



# National Patient Safety Agency

National Research Ethics Service

## NOTICE OF SUBSTANTIAL AMENDMENT

For use in the case of all research other than clinical trials of investigational medicinal products (CTIMPs). For substantial amendments to CTIMPs, please use the EU-approved notice of amendment form (Annex 2 to ENTR/CT1) at <http://eudract.emea.eu.int/document.html#guidance>.

To be completed in typescript by the Chief Investigator in language comprehensible to a lay person and submitted to the Research Ethics Committee that gave a favourable opinion of the research ("the main REC"). In the case of multi-site studies, there is no need to send copies to other RECs unless specifically required by the main REC.

Further guidance is available at <http://www.nres.npsa.nhs.uk/applicants/review/after/amendments.htm>.

### Details of Chief Investigator:

Name:	Professor Christopher EM Griffiths
Address:	Dermatology Centre Hope Hospital Stott Lane Salford
Telephone:	0161 206 4392
Email:	christopher.griffiths@manchester.ac.uk
Fax:	0161 206 1095

<b>Full title of study:</b>	British Association of Dermatologists' Biological Interventions Register
<b>Name of main REC:</b>	North West England
<b>REC reference number:</b>	07/MRE08/9
<b>Date study commenced:</b>	16/08/07
<b>Protocol reference (if applicable), current version and date:</b>	BADBIR Study Protocol – Version 12 (30/11/2007)
<b>Amendment number and date:</b>	Amendment Four (revised 30/10/09) 24/12/08

**Type of amendment (indicate all that apply in bold)**

(a) Amendment to information previously given on the NRES Application Form

**Yes**

*If yes, please refer to relevant sections of the REC application in the "summary of changes" below.*

(b) Amendment to the protocol

**Yes**

*If yes, please submit either the revised protocol with a new version number and date, highlighting changes in bold, or a document listing the changes and giving both the previous and revised text.*

(c) Amendment to the information sheet(s) and consent form(s) for participants, or to any other supporting documentation for the study

**Yes**

*If yes, please submit all revised documents with new version numbers and dates, highlighting new text in bold.*

**Is this a modified version of an amendment previously notified to the REC and given an unfavourable opinion?**

Yes

**Summary of changes**

*Briefly summarise the main changes proposed in this amendment using language comprehensible to a lay person. Explain the purpose of the changes and their significance for the study. In the case of a modified amendment, highlight the modifications that have been made.*

If the amendment significantly alters the research design or methodology, or could otherwise affect the scientific value of the study, supporting scientific information should be given (or enclosed separately). Indicate whether or not additional scientific critique has been obtained.

**a) MREC application form**

Professor Alan Silman is no longer a Principal Investigator

Section A10 (1) page 8 Methodology for collection of patient reported questionnaires  
**Problem**

Questionnaire response rates across centres are 62% at baseline. This is in line with postal administration in other studies and is likely to decrease over the five-year follow-up period. Response rates in a similar register (British Society for Rheumatology Biologics Register, BSRBR) are higher, approximately 75%. The gender difference between the two populations may partially explain this difference in response rates<sup>1</sup> (RA patient population

predominantly female - females are more likely to complete questionnaires)  
However, the BSRBR team report anecdotally there are problems with the interpretation of the patient reported data as some of it is difficult to interpret and hence difficult to use effectively in analysis. BSRBR would not chose the mailing option of these questionnaires if the register was starting today

#### Proposed change

1. The questionnaires are given to the patient for completion in the waiting area prior to the consultation.
2. Clinician checks the level of completion before entering data onto the web.
3. Clinician provides 6 monthly diaries to the patient at each visit. The patient returns the diary at each follow-up visit.
4. Clinician checks the diary entries with the patient and clarifies as appropriate.

#### Positive aspects to proposed change in methodology

1. The proportion of missing data will decrease thereby enhancing the validity of the findings.
2. Discussion of the diary contents with a clinician will improve the collection of adverse event data as any incongruous reporting will be clarified immediately at source.
3. Checking and discussing this data with the patient would allow for enhanced communication during the consultation process and may improve the quality of the clinical consultation. <sup>2</sup>
4. This will not increase the patient burden as the time taken to complete these questionnaires in clinic should not be different to completion at home. In addition, this procedure will remove the burden of posting the questionnaires back to the University of Manchester by the patient. As most patients spend at least 10 minutes waiting to see a doctor/nurse this change in procedure would not be expected to increase the total clinic visit time.

#### Potential negative aspects to proposed change in methodology

Increased burden on dermatology team although there is funding available to reimburse time spent on this additional task.

1. Impact of chronic disease on quality of life in the Bella Coola Valley. Thommasen HV, Zhang W. Rural Remote Health. 2006 Apr-Jun; 6(2):528. Epub 2006 Jun 5.

2. The practical reality of using a patient-reported outcome measure in a routine dermatology clinic. Salek S, Roberts A, Finlay AY. Dermatology. 2007; 215(4):315-9.

#### **b) Protocol amendments**

The protocol has been amended (amended text in bold font) for two reasons

1. To reflect the original MREC application and change in personnel since application
2. To include suggestions from the Steering Group and the principal investigators

1. Study Team (protocol page 1)

Chief Investigator	Prof Chris Griffiths
Principal Investigator	Dr A.D. Ormerod
Principal Investigator	Prof Deborah Symmons
Study Co-ordinator	Dr Kathleen McElhone

2.

a) The following amendments have been made to clarify the inclusion criteria in both cohorts.

*Section 3.2.1 (page 6)*

i. Biologic Cohort Inclusion criteria

To ensure consistency with the inclusion criteria of the conventional cohort "Patients commencing treatment with a biological agent in the previous six months for their psoriasis" has been amended to

"Patients commencing or **switching** treatment with a biological agent in the previous six months for their psoriasis"

*Section 3.2.2 (page 6)*

ii. Conventional cohort Inclusion criteria

Hydroxycarbamide is considered to be a standard therapy for psoriasis and as such as been added to the list of eligible treatments

b) Section 6 Summary Study Flow Chart (page 10)

CAGE has been changed in the table to "if applicable" as it is not relevant to all patients e.g. Patients who do not drink for religious or cultural reasons?

The Patient Information Leaflet has been amended

a) to correct errors and omissions

i) Study Title: British Association of Dermatologists' Biological Interventions Register

ii) Pharmaceutical "studies" should be pharmaceutical "companies"

b) to reflect organisational change i.e. the "National Health Service Information Centre" is now the body who undertake flagging for the occurrence of malignancy or death instead of the "Office of National Statistics"

c) to more accurately reflect the audit procedure

"Your medical records will state that you are in this Register. By signing the consent form, you are allowing the dermatology team to permit the University of Manchester or independent companies monitoring the study and auditing the results on behalf of the University of Manchester to have access to your medical records relevant to the Register."

"In certain circumstances your medical records or study data may be looked at by a government drug regulatory agency or by authorised members of the Ethics Committee or Hospital. This is for the purpose of, checking that the data is correct or checking that the Register is being done properly."

d) To inform the patient of the potential for their anonymised data to be transferred outside the European Union.

"This study is being conducted according to the requirements of the UK Data Protection Act 1998. By signing the consent form you are agreeing that your medical information from the Register may be sent outside the Europe for analysis in a form that does not include your name."

The Informed Consent Form has also been changed to reflect these changes.

**Any other relevant information**

*Applicants may indicate any specific ethical issues relating to the amendment, on which the opinion of the REC is sought.*

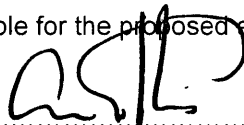
**List of enclosed documents**

<i>Document</i>	<i>Version</i>	<i>Date</i>
BADBIR	13	24/12/08
Patient Information Leaflet	4	24/12/08
Patient Consent Form	4	24/12/08

**Declaration**

- I confirm that the information in this form is accurate to the best of my knowledge and I take full responsibility for it.
- I consider that it would be reasonable for the proposed amendment to be implemented.

Signature of Chief Investigator: .....



Print name: .....

Prof Cem Suffith

Date of submission: .....

5.11.09